PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 13453-62PCT	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/CA2005/000472	International filing date *(day/month/year)* 30 March 2005 (30-03-2005)	Priority date *(day/month/year)* 30 March 2004 (30-03-2004)

International Patent Classification (IPC) or national classification and IPC
IPC: ***A61K 39/395*** (2006.01) , ***A61K 39/00*** (2006.01) , ***A61P 37/00*** (2006.01)

Applicant
CANADIAN BLOOD SERVICES ET AL

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. [X] *(sent to the applicant and to the International Bureau)* a total of 13 sheets, as follows:

      [X] sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      [ ] sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. 1 and the Supplemental Box.

   b. [ ] *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))
      , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

   [X] Box No. I Basis of the report
   [X] Box No. II Priority
   [X] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   [ ] Box No. IV Lack of unity of invention
   [X] Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   [ ] Box No. VI Certain documents cited
   [ ] Box No. VII Certain defects in the international application
   [X] Box No. VIII Certain observations on the international application

Date of submission of the demand 30 January 2006 (30-01-2006)	Date of completion of this report 28 July 2006 (28-07-2006)
Name and mailing address of the IPEA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001(819)953-2476	Authorized officer Qianfa Chen (819) 994-1374

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/CA2005/000472

Box No. I Basis of the report

1. With regard to the **language,** this report is based on:

[X] the international application in the language in which it was filed

[ ] a translation of the international application into , which is the language of a translation furnished for the purposes of:

[ ] international search (Rules 12.3(a) and 23.1(b))

[ ] publication of the international application (Rule 12.4(a))

[ ] international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

[ ] the international application as originally filed/furnished

[X] the description:

[X] pages 1, 3-6, 8-26, 30 and 31 as originally filed/furnished

[X] pages* 2 and 27-29 received by this Authority on 30 January 2006 (30-01-2006)

[X] pages* 7 received by this Authority on 07 July 2006 (07-07-2006)

[X] the claims:

[ ] pages as originally filed/furnished

[ ] pages* as amended (together with any statement) under Article 19

[X] pages* 32-39 containing claims 1-62 received by this Authority on 11 July 2006 (11-07-2006)

[ ] pages* received by this Authority on

[X] the drawings:

[X] pages 1/14-14/14 as originally filed/furnished

[ ] pages* received by this Authority on

[ ] pages* received by this Authority on

[ ] a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/figs

[ ] the sequence listing *(specify):*

[ ] any table(s) related to sequence listing *(specify):*

4. [ ] This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/figs

[ ] the sequence listing *(specify):*

[ ] any table(s) related to sequence listing *(specify):*

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. II Priority

1. [ ] This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

   [ ] copy of the earlier application whose priority has been claimed (Rule 66.7(a)).

   [ ] translation of the earlier application whose priority has been claimed (Rule 66.7(b)).

2. [ ] This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

The priority document has been found to provide support for claims 1-62.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The question whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

[ ] the entire international application

[X] claims Nos. 1-32

because:

[X] the said international application, or the said claims Nos. 1-32
relate to the following subject matter which does not require an international preliminary examination *(specify):*

Claims 1-32 are directed to a method for treatment of the human or animal body by surgery or therapy, are not required to be searched nor is a written opinion required by this Authority under Rule 67.1 (iv) of the PCT. Regardless, this Authority has established an IPRP based on the alleged effect(s) or purpose(s)/use(s) of the product defined in claims 1-32.

[ ] the description, claims or drawings *(indicate particular elements below)* or said claims Nos.
are so unclear that no meaningful opinion could be formed *(specify):*

[ ] the claims, or said claims Nos.
by the description that no meaningful opinion could be formed *(specify):*
are so inadequately supported

[ ] no international search report has been established for said claims Nos.

[ ] a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

[ ] furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

[ ] furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

[ ] pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

[ ] a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

[ ] the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

[ ] See Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/CA2005/000472

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-62	YES
	Claims		NO
Inventive step (IS)	Claims	1-62	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-62	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Reference is made to the following documents (cited in the ISR):

D1: WO 99/03495 A1 (AVRAHAM, H. and GROOPMAN J.E.), 28 January 1999.

D2: WO 02/40047 A2 (LAZARUS, A. et al.), 23 May 2002.

D3: SONG, S. et al. Blood. 1 May 2003. Vol.101, No.9, pages 3708-3713.

Novelty and Inventive Steps

Claims 1-62 meet the criteria set out in Articles 33(2) and 33(3) of the PCT, because the closest prior art (D1, D2 or D3) does not teach a method, a composition or use thereof, for treating an immune thrombocytopenia or inflammatory arthritis, or for inhibiting platelet clearance in a patient by means of an in *vivo* antibody-antigen interaction without invoking the biological function of the antigen, wherein the administration of the antibody and/or the soluble antigens result in the selective binding of said antibody and said soluble antigen, and wherein said antigen is substantially soluble in vivo.

The closest prior art (D1, D2 or D3) describes the therapeutical application of monoclonal antibodies for treating auto-immune thrombocytopenic purpura (ITP) in a patient. Examples of the monoclonal antibodies include an anti-megakaryocytic cells antibody (anti-c-Mpl) in D1, anti-red blood cell antibodies (anti-CD24 and anti- TER-119) in D2 or D3, an anti-leukocyte antibody (anti-CD44) in D2 or D3, and a monoclonal antibody anti-CD16/32 in D3. Although the soluble form of each of the antigen proteins of c-Mpl, CD24, TER-119 , CD44 and CA16/32 of D1, D2 or D3 has been detected previously, the soluble form of the above antigen proteins only represents a small percentage of the antigen proteins in vivo. Majority of each of the above antigen proteins of D1, D2 or D3 are present on the cell surface and are not substantially soluble in vivo.

Industrial Applicability

Claims 1-62 have industrial applicability as defined under Article 33(4) of the PCT.

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim Defects

Claims 1, 18, 33 and 48, when the expression "and/or" is "or", are broader in scope than the teaching of the description and do not comply with Article 6 of the *Patent Cooperation Treaty (PCT)*. The claimed method, composition and use thereof encompass subject matter that is not contemplated in the description by the applicant. The instant description on page 14, lines 17-19 indicates that ovalbumin (OVA, a foreign antigen) incubated with anti-OVA antibodies was capable of inhibiting ITP. However, the instant description on page 14, lines 20-26 also describes that "mice treated with soluble OVA alone (Figure 3A&B, 0.0 mg/mouse) or OVA + control IgG (data not shown) were not significantly protected from the development of immune thrombocytopenia. OVA by itself did not affect the platelet count at any dose tested (0.1 mg, 1 mg, 5 mg and 10 mg, data not shown). Similarly, all of the anti-OVA antibodies, in the absence of OVA, did not inhibit immune thrombocytopenia (data not shown)". This clearly suggests that neither a foreign antigen in the absence of an antibody specific thereto, nor an antibody specific for a soluble foreign antigen in the absence of the foreign antigen is capable of treating ITP. Therefore, a claim to a method or composition for treating ITP by administering an effective amount of an antibody specific for a soluble antigen, **or** a complementary soluble antigen thereof, without defining that the antibody specific for the soluble antigen is incubated with the soluble antigen prior to the administering, is not supported in the description as filed.

The present study was undertaken to investigate if antibodies to soluble antigens could inhibit autoimmune diseases.

SUMMARY OF THE INVENTION

According to the present invention, a novel method for treating an autoimmune disease is provided. Furthermore, a novel mechanism of action has been established in accordance with the present invention for antibody-based treatment regimes for autoimmune disease, including, but not limited to anti-CD44 and soluble antigen specific antibody treatment regimes.

In one embodiment of the invention there is provided a method for treating autoimmune diseases in a mammal which method comprises administering to the mammal an effective amount of at least one antibody specific for a soluble antigen.

Different types of autoimmune diseases can be treated by the method of the present invention. According to the present invention, an autoimmune disease includes, but is not limited to Immune thrombocytopenia, Immune cytopenia, Idiopathic thrombocytopenic purpura (ITP), Neuropathy, Chronic inflammatory demyelinating polyneuropathy (CIDP), Guillain-Barre syndrome (GBS), Kawasaki's disease, Dermatomyositis, SLE, Myasthenia gravis, Post-transfusion purpura, Rheumatoid arthritis, Inflammatory arthritis, Eaton-Lambert syndrome,toxic epidermal necrolysis, and polymyositis.

In one embodiment, the treatment can be effected for a time and under conditions sufficient to inhibit platelet clearance, thereby treating or ameliorating an autoimmune disease such as immune thrombocytopenic purpura (ITP), for example. In a further embodiment, inflammatory arthritis can

thrombocytopenia. Mice injected with soluble ovalbumin (OVA) or OVA conjugated to RBCs (OVA-RBC) in the presence of anti-OVA, were both significantly protected from immune thrombocytopenia.

Both of these therapeutic regimes functioned independent of complement activity and both regimes also blocked reticuloendothelial function as assessed by clearance rates of fluorescent sensitized syngeneic RBCs. Soluble OVA or anti-OVA alone did not have any direct effect on immune thrombocytopenia in mice. It was found that OVA-RBC + anti-OVA ameliorated immune thrombocytopenia in normal mice and FcγRIIB$^{-/-}$ mice, while soluble OVA + anti-OVA was ineffective in FcγRIIB$^{-/-}$ mice. In addition, IgG specific for murine albumin and specific for transferrin also effectively inhibited ITP. Thus, IgG antibodies directed to soluble antigens can inhibit or reverse immune thrombocytopenia in an FcγRIIB-dependent manner, whereas antibodies directed to a cell-associated antigen function independent of FcγRIIB expression.

Materials and Methods:

Reagents:

The monoclonal antibody specific for integrin α_{IIb} (rat $IgG_{1\kappa}$, clone MWReg 30) was purchased from BD Pharmigen (Mississauga, ON, Canada). Monoclonal murine anti-OVA (IgG_1, clone OVA-14), rabbit polyclonal anti-OVA, 1-ethyl-3-(3-dimethylamino-propyl) carbodiimide (EDAC), OVA (grade V), and PKH26 red fluorescent cell linker kit were purchased from Sigma (Oakville, ON, Canada). IVIG was Gamimune,10% from Bayer (Elkhart, IN). Cobra Venom Factor (CVF), FITC-conjugated $F(ab')_2$ anti-rabbit IgG, and control rabbit IgG, were purchased from Cedarlane Laboratories Ltd (Hornby, ON, Canada). Rabbit anti-mouse albumin (IgG fraction), and rabbit anti-mouse transferrin (IgG fraction), were purchased from Research

experimental evidence that the antibody-based treatment regimes of the present invention, induce a priming event in innate leukocytes which endows leukocytes with the ability to ameliorate or inhibit autoimmune disease, specifically in ITP, thrombocytopenia, or in inflammatory arthritis, joint inflammation. We call this effect "IVIg-mediated cellular programming" (IMCP). This term is intended to more broadly refer to an antibody-mediated cellular programming effect, however for simplicity reference is made to the IVIg example, and hence IMCP is used throughout without prejudice. It is not intended to restrict the effect to only IVIg treatment regimes.

A monoclonal antibody (anti-CD44) is also demonstrated to inhibit immune thrombocytopenia by the same mechanism (ie. an IMCP-like effect in Figure 11. Here, anti-CD44 + leukocytes were incubated for 30 min, unbound anti-CD44 was washed off, leukocytes were then injected into ITP mice, and an amelioration of thrombocytopenia resulted. Mice in the first column (Nil) were uninjected. Mice in the second column (ITP) were treated with anti-platelet antibody (αCD41) only. On Day 1, mice in the third and fourth column (IMCP) were injected intravenously with splenic leukocytes (106/mouse) that went through the IMCP process with IVIg or anti-CD44 for 30 min. On Day 2 mice in columns (second to fourth) were injected with 2 µg anti-platelet antibody. On Day 3, all mice were bled for platelet enumeration as described (Blood 105:1546-1548, 2005).

Figure 12 illustrates an antibody-mediated cellular programming effect, herein referred to as IMCP, as mentioned above, at work in splenic leukocytes incubated with monoclonal anit-OVA, thus establishing a basis for the mode of action of the treatment regimes of the present invention. As illustrated, anti-ovalbumin + ovalbumin + leukocytes are

incubated for 30 min, unbound anti-ovalbumin and ovalbumin are washed off, and leukocytes are injected into ITP mice to provide ameliorating effect against thrombocytopenia in vivo. According to Figure 12, mice in the first column (Nil) were uninjected. Mice in the second column (ITP) were treated with anti-platelet antibody (αCD41) only. On Day 1, mice in the third column (IVIg) were injected with 50 mg/ml of dialyzed IVIg. Mice in the fourth column were injected (i.v.) with 1 mg OVA that had been pre-incubated with 50 μg of monoclonal anti-OVA (IgG1, clone OVA-14 Sigma). Mice in the fifth column were treated as in fourth column except with control mouse IgG (mouse IgG, Cat# 10400, Caltag) in place of monoclonal anti-OVA. Mice in the sixth column (IMCP) were injected intravenously with splenic leukocytes (106/mouse) that went through the IMCP process with dialyzed IVIg for 30 min. Mice in the seventh column were treated with splenic leukocytes (106/mouse) that went through IMCP process with 1 mg OVA that had been pre-incubated with 50 μg of monoclonal anti-OVA for 30 min. Mice in the eigth column were treated as in seventh column except with control mouse IgG in place of monoclonal-anti-OVA. On Day 2, mice in columns (second to eigth) were injected with 2 μg anti-platelet antibody. On Day 3, all mice were bled for platelet enumeration as described (Blood 102:558-560, 2003).

IVIg, anti-CD44 (KM-114), and antibody to soluble antigens (in the presence of the soluble antigen) cannot ameliorate thrombocytopenia in mice which are genetically deficient in the inhibitory Fcγ receptor (FcγRIIB) Interestingly, however, we show here that these same antibodies can, all ameliorate thrombocytopenia when they are pre-incubated with leukocytes isolated from mice that are genetically deficient in FcγRIIB ($Fc\gamma RIIB^{-/-}$) and the $Fc\gamma RIIB^{-/-}$

leukocytes are injected into wild type mice. Thus, the IMCP effect as herein reported can work where leukocytes do not express an FcgammaRIIB receptor. Although, FcgammaRIIB receptor expression was required in the recipient in order to achieve IMCP. In the reverse of this experiment (where the leukocytes are from FcγRIIB$^{+/+}$ mice and the recipient mice are FcγRIIB$^{-/-}$), again, IVIg, anti-CD44, and anti-soluble antigen (+ the antigen) all cannot ameliorate the thrombocytopenia (Figure 13). As shown in Figure 13, mice in the 1st column (Nil-BL/6) are uninjected C57BL/6 mice. Mice in the 2nd column (CD41-BL/6) were C57BL/6 mice treated with anti-platelet antibody (αCD41) only. Mice in the 8th column (Nil-RIIB) were uninjected FcγRIIB$^{-/-}$ mice. Mice in the 9th column (CD41-RIIB) were FcγRIIB$^{-/-}$ mice treated with anti-platelet antibody (αCD41) only. On Day 1, mice in the 3rd column (IVIG-BL/6) were injected with 50 mg/ml IVIg. Mice in the fourth column (IVIG-BL/6) were C57BL/6 mice injected intravenously with splenic leukocytes (10^6/mouse) from C57BL/6 mice that went through the IMCP process with IVIg for 30 min. Mice in the 5th column (IVIG-RIIB) were FcγRIIB$^{-/-}$ mice injected intravenously with splenic leukocytes (10^6/mouse) from C57BL/6 mice that went through the IMCP process with IVIg for 30 min. Mice in the 6th column (BSA-RIIB) were FcγRIIB$^{-/-}$ mice injected intravenously with splenic leukocytes (10^6/mouse) from C57BL/6 mice that went through the IMCP process with BSA for 30 min. Mice in the 7th column (BSA-BL/6) were C57BL/6 mice injected intravenously with splenic leukocytes (10^6/mouse) from C57BL/6 mice that went through the IMCP process with BSA for 30 min. Mice in the 10th column (IVIG-RIIB) were injected with 50 mg/ml IVIg. Mice in the 11th column (IVIG-BL/6) were C57BL/6 mice injected intravenously with splenic leukocytes (10^6/mouse) from FcγRIIB$^{-/-}$ mice that went through the IMCP process with IVIg for 30 min. Mice in the 12th column (IVIG-RIIB) were FcγRIIB$^{-/-}$ mice

I/WE CLAIM:

1. A method for treating an immune thrombocytopenia or inflammatory arthritis in a mammal by means of an in vivo antibody-antigen interaction, without invoking the biological function of the antigen, which method comprises administering to said mammal an effective amount of at least one IgG antibody and/or a complementary soluble antigen thereof, wherein said administration results in the selective binding of said antibody with said soluble antigen in vivo in said mammal, and wherein said antigen is substantially soluble in vivo.

2. The method as claimed in claim 1 wherein said soluble antigen is a foreign antigen.

3. The method as claimed in claim 2 wherein said soluble foreign antigen is administered to said mammal prior to or following administering said antibody.

4. The method as claimed in claim 2 wherein said soluble foreign antigen and said antibody are incubated together to form antibody-antigen conjugates prior to administering said conjugates to said mammal.

5. The method as claimed in claim 3 or 4 wherein said foreign antigen is ovalbumin.

6. The method as claimed in claim 2 wherein said mammal has a pre-existing IgG to said soluble antigen and an effective amount of said soluble antigen is administered.

7. The method as claimed in claim 2 wherein said antibody is monoclonal or polyclonal.

8. The method as claimed in claim 1 wherein said soluble antigen is endogenous.

9. The method as claimed in claim 8 wherein an effective amount of said antibody is administered.

10. The method as claimed in claim 8 wherein said endogenous soluble antigen is obtained from said mammal and incubated with said antibody to form antibody-antigen conjugates, said conjugates being administered to said mammal.

11. The method as claimed in claim 8 wherein said soluble endogenous antigen is selected from albumin, transferrin and combinations thereof.

12. The method as claimed in claim 8 wherein said antibody is a polyclonal antibody or monoclonal antibody.

13. The method as claimed in claim 1 wherein said mammal is a human or a non-human mammal.

14. The method according to claim 1, wherein said at least one antibody and/or soluble antigen is administered intravenously, interperitoneally, intradermally, intramuscularly, subcutaneously, orally or rectally.

15. The method of claim 1 wherein said at least one antibody and/or soluble antigen is administered for a time and under conditions sufficient to inhibit platelet clearance.

16. The method of claim 1 for treating an immune thrombocytopenia.

17. The method of claim 1 for treating inflammatory arthritis.

18. A method of inhibiting platelet clearance in a patient in need thereof by means of an in vivo antibody-antigen interaction, without invoking the biological function of the antigen, which method comprises administering to the patient a composition comprising a therapeutic amount of at least one IgG antibody and/or a complementary soluble antigen thereof, and a pharmaceutically acceptable carrier, wherein said administration results in the selective binding of said antibody with said soluble antigen in said patient, and wherein said antigen is substantially soluble in vivo..

19. The method of claim 18, wherein the therapeutic amount of the at least one antibody ranges from about 0.1µg to about 1g per kg of body weight per day.

20. The method of claim 18, wherein the at least one antibody and/or soluble antigen is administered for a time sufficient to therapeutically increase and maintain platelet cell counts.

21. The method as claimed in claim 18 wherein said soluble antigen is a foreign antigen.

22. The method as claimed in claim 21 wherein said soluble antigen is administered to said mammal prior to or following administering said antibody.

23. The method as claimed in claim 21 wherein said soluble antigen and said antibody are incubated together to form antibody-antigen or antibody-antigen-blood cell conjugates prior to administering said conjugates to said mammal.

24. The method as claimed in claim 21 wherein said soluble antigen is ovalbumin.

25. The method as claimed in claim 21 wherein said mammal has a pre-existing IgG to said soluble antigen and an effective amount of said soluble antigen is administered.

26. The method as claimed in claim 21 wherein said antibody is monoclonal or polyclonal.

27. The method as claimed in claim 18 wherein said soluble antigen is endogenous.

28. The method as claimed in claim 27 wherein said soluble antigen is selected from albumin, transferrin and combinations thereof.

29. The method as claimed in claim 27 wherein an effective amount of said antibody is administered.

30. The method as claimed in 27 wherein said soluble antigen is obtained from said mammal and incubated with said antibody to form antibody-antigen conjugates, said conjugates being administered to said mammal.

31. The method as claimed in claim 18 wherein said mammal is a human or a non-human mammal.

32. The method according to claim 18, wherein said at least one antibody and/or soluble antigen is administered intravenously, interperitoneally, intradermally, intramuscularly, subcutaneously, orally or rectally.

33. A pharmaceutical composition for treating an immune thrombocytopenia or inflammatory arthritis by means of an in vivo antibody-antigen interaction, without invoking the biological function of the antigen, said composition comprising an effective amount of at least one IgG antibody and/or a complementary soluble antigen

thereof in combination with a pharmaceutically acceptable carrier, wherein administration of said composition results in the selective binding of said antibody with said soluble antigen in vivo in said mammal, and wherein said antigen is substantially soluble in vivo.

34. The composition as claimed in claim 33, wherein said antibody and/or soluble antigen is capable of inhibiting platelet clearance.

35. The composition as claimed in claim 33 wherein said soluble antigen is a foreign antigen..

36. The composition as claimed in claim 35 wherein said composition comprises said soluble antigen for administration to said mammal prior to or following administering said antibody.

37. The composition as claimed in claim 35 wherein said composition comprises said soluble foreign antigen and said antibody as antibody-antigen or antibody-antigen-blood cell conjugates for administering said conjugates to said mammal.

38. The composition as claimed in claim 36 or 37 wherein said foreign antigen is ovalbumin.

39. The composition as claimed in claim 35 wherein said mammal has a pre-existing IgG to said soluble antigen and said composition comprises an effective amount of said soluble antigen.

40. The composition as claimed in claim 35 wherein said antibody is monoclonal or polyclonal.

41. The composition as claimed in claim 33 wherein said soluble antigen is endogenous.

42. The composition as claimed in claim 41 wherein said composition comprises an effective amount of said antibody.

43. The composition as claimed in claim 41 wherein said soluble endogenous antigen is selected from albumin, transferrin and combinations thereof.

44. The composition as claimed in 41 wherein said composition comprises said endogenous soluble antigen obtained from said mammal and said antibody as antibody-antigen conjugates for administering said conjugates to said mammal.

45. The composition as claimed in claim 33 wherein said mammal is a human or a non-human mammal.

46. The composition as claimed in claim 33, wherein said composition is formulated for administration intravenously, intradermally, interperitoneally, intramuscularly, subcutaneously, orally or rectally.

47. The composition as claimed in claim 33, wherein said at least one antibody and/or soluble antigen is capable of inhibiting platelet clearance.

48. Use of at least one IgG antibody and/or a complementary soluble antigen thereof for the manufacture of a medicament for the treatment of an immune thrombocytopenia or inflammatory arthritis by means of an in vivo antibody-antigen interaction, without invoking the biological function of the antigen, wherein said use results in the selective binding of said

antibody with said soluble antigen in vivo in said mammal, and wherein said antigen is substantially soluble in vivo.

49. The use of claim 48 wherein said medicament comprises a therapeutic amount of said at least one antibody and/or soluble antigen effective to slow or inhibit platelet clearance when administered to a patient in need thereof.

50. The use of claim 49 wherein the therapeutic amount of said at least one antibody is from about 0.1µg to about 1g per kg of body weight per day.

51. The use as claimed in claim 48 wherein said soluble antigen is a foreign antigen.

52. The use as claimed in claim 51 wherein said soluble foreign antigen is for administration to said mammal prior to or following administration of said antibody.

53. The use as claimed in claim 51 wherein said soluble foreign antigen and said antibody are incubated together to form antibody-antigen or antibody-antigen-blood cell conjugates for manufacturing the medicament.

54. The use as claimed in claim 52 or 53 wherein said foreign antigen is ovalbumin.

55. The use as claimed in claim 51 wherein said mammal has a pre-existing IgG to said foreign soluble antigen and said foreign soluble antigen is for manufacturing the medicament.

56. The use as claimed in claim 51 wherein said antibody is monoclonal or polyclonal.

57. The use as claimed in claim 48 wherein said soluble antigen is endogenous.

58. The use as claimed in claim 57 wherein said soluble endogenous antigen is selected from albumin, transferrin and combinations thereof.

59. The use as claimed in claim 57 wherein said antibody is used for manufacturing the medicament.

60. The use as claimed in claim 57 wherein said endogenous soluble antigen is obtained from said mammal and incubated with said antibody to form antibody-antigen conjugates, said conjugates being used for manufacturing the medicament.

61. The use as claimed in claim 48 wherein said mammal is a human or a non-human mammal.

62. The use as claimed in claim 48 wherein said at least one antibody and/or soluble antigen is formulated for administration intravenously, interperitoneally, intradermally, intramuscularly, subcutaneously, orally or rectally.

AMENDED SHEET